A rapid and efficient synthesis of thiochroman-4-ones under microwave irradiation

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Thiochroman-4-ones were synthesised by the cyclization of β-arylthiopropionic acids which were prepared by the condensation of the arylthiols with chloropropionic acid under microwave irriadiation within 4min.

Keywords: thiochroman-4-one, arylthiol, chloropropionic acid

Benzothiopyran-4-ones have attracted considerable attention due to their effective antifungal activity.[1,2] They are also useful and versatile building blocks for the synthesis of important benzothiopyran compounds.[3,4] These compounds are commonly synthesised *via* the reaction of methyl acrylate with arylthiols catalysed by sodium methoxide,[5] or *via* the cyclisation of arylthiopropionic acid using concentrated H_2SO_4 as dehydrating agent.[6] However, the procedures mentioned above suffer from drawbacks such as longer reaction times, cumbersome product isolation procedures and serious decomposition.[7-13]

Microwave heating and its application in organic synthesis have been reviewed.[14] Many papers concerning rate enhancement in many reactions have been reported.[15] Recently we have described the sulfonation of aromatic amines with sulfuric acid under microwave irradiation to give amino sulfonic acids in good yields.[16] All of the results stated above prompted us to study the possibility for the synthesis of β-arylthiopropionic acids and thiochroman-4-ones under microwave irradiation. We now report a convenient and efficient synthesis of β-arylthiopropionic acids and thiochroman-4-ones from chloropropionic acid and arylthiols under microwave irradiation (Scheme 1).

As shown in Table 1, under microwave irradiation, the condensation of chloropropionic acid and arylthiols was carried out in 78–90% yields within 3–4 min. The cyclisation of arylthiopropionic acid was carried out in 77–90% yields. Compared with classical methods, the main advantages of the present procedure are easy work-up, excellent yield and shorter time. For example, *p*-methylphenylthiopropionic acid (**2e**) was obtained in 78% yield by refluxing for 2 h in EtOH,[10] whereas, the present method offered the product in 85% yield within 3.5 min. Thiochroman-4-ones were prepared in 71–80% yields by stirring for 4–6 h in benzene at refluxing temperature, but the present procedure give the product in 77–90% yields within only 1–2 min under microwave irradiation. Additionally, phosphoric acid produced in the cyclisation can be used to acidify the reaction mixture in the first step.

In conclusion, we have described a rapid and efficient procedure for the synthesis of thiochroman-4-ones and arylthiopropionic acid under microwave irradiation.

Table 1 Synthesis of the β-arylthiopropionic acids and thiochroman-4-ones under microwave irradiation

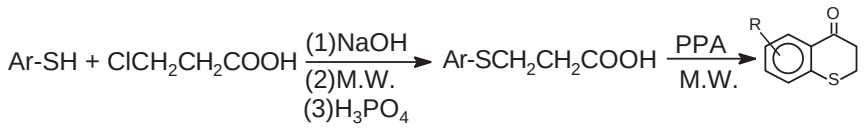
Entry	Ar	Power/%	Time/min	Yield/%	M.p./°C (Lit.)
2a	C_6H_5	60	3.5	86	59 (59)[6]
2b	4-FC_6H_4	60	4	78	76 (72-73)[12]
2c	4-ClC_6H_4	60	4	87	91–93(90–91)[10]
2d	4-BrC_6H_4	60	4	81	114–116(114–115)[10]
2e	4-$CH_3C_6H_4$	60	3.5	85	71 (71–72)[6]
2f	4-$CH_3OC_6H_4$	60	3	90	83–84(81–82)[10]
2g	4-$CH_3SC_6H_4$	60	3.5	82	105–106(106–107)[10]
3a	C_6H_5	20	1	80	29(29–30)[6]
3b	4-FC_6H_4	20	2	77	96(96–97)[12]
3c	4-ClC_6H_4	20	2	81	69–71(67–69)[10]
3d	4-BrC_6H_4	20	2	83	72(70–71)[10]
3e	4-$CH_3C_6H_4$	20	1	85	40(41–42)[6]
3f	4-$CH_3OC_6H_4$	20	1	90	28–31(29–30)[10]
3g	4-$CH_3SC_6H_4$	20	1	84	75–76(76–77)[10]

Experimental

The starting materials are chemically pure reagents (except for PPA). Melting points were uncorrected and were measured with micro-melting point apparatus. The reactions were carried out in a SHARP-WP850A microwave oven. IR spectra were measured on a Bio-Rad FTS-40-spectrometer (KBr); ^{1}H NMR spectra were recorded on AVANCE-400S (400MHz) spectrometer using $CDCl_3$ as a solvent and TMS as internal standard.

General procedure for the preparation for β-*arylthiopropionic acid:* A wet solid mixture of sodium arylthiolate and sodium β-chloropropionate was obtained by neutralisation of a mixture of (50 mmol) and β-chloropropionic acid (50 mmol) by 50% aqueous sodium hydroxide (5 ml) and evaporation of water in conical flask. The mixture was irradiated for a period as indicated in Table 1 in a commercial microwave oven and then, was dissolved in a minimum of water, acidified to pH=3 with phosphoric acid (about 25 ml) and collected by filtration. The product was recrystallised from H_2O-EtOH (5:1). The authenticity of the products was established by comparing their melting points with the literature.

General procedure for the preparation for thiochroman-4-one: A mixture of β-arylthiopropionic acids (1g) and polyphosphoric acid (52g P_2O_5 and 36 ml 85% H_3PO_4) (10g) in the breaker, was irradiated (1–2 min) in the commercial microwave oven and then was poured into crushed ice, the sediment was filtered and washed by 5% aqueous Na_2CO_3. The crude product was recrystallised from MeOH to give the corresponding thiochroman-4-one. The authenticity of the products was established by comparing their melting points with the literature and the data of IR, ^{1}H NMR spectra.



1 (a-g) **2 (a-g)** **3 (a-g)**

Scheme 1

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3a: IR(KBr): 1660 (C=O), 1595, 1430 (C_6H_6) cm^{-1}; ^1H NMR($CDCl_3$, δ): 8.05(1H, s, ArH), 7.30(1H, d, *J*=8.6 Hz, ArH), 7.25(1H, d, *J*=8.6 Hz, ArH), 7.10(1H, d, *J*=8.6 Hz, ArH), 2.90(2H, m, CH_2), 3.18(2H, m, CH_2)ppm.

3b: IR(KBr): 1670 (C=O), 1585, 1430 (C_6H_6) cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.83(1H, s, ArH), 7.30(1H, d, *J*=7.2 Hz, ArH), 7.30(1H, d, *J*=7.2 Hz, ArH), 3.00(2H, t, CH_2), 3.24(2H, t, CH_2)ppm.

3c: IR(KBr): 1670 (C=O), 1585, 1430 (C_6H_6) cm^{-1}; H^1 NMR ($CDCl_3$, δ): 8.00(1H, s, ArH), 7.35(1H, d, *J*=7.8 Hz, ArH), 7.15(1H, d, *J*=7.8 Hz, ArH), 2.90(2H, m, CH_2), 3.18(2H, m, CH_2)ppm.

3d: IR(KBr): 1670 (C=O), 1585, 1430 (C_6H_6) cm^{-1}; H^1 NMR ($CDCl_3$, δ): 8.00(1H, s, ArH), 7.35(1H, d, *J*=8.4 Hz, ArH), 7.15(1H, d, *J*=8.4 Hz, ArH), 2.99(2H, m, CH_2), 3.20(2H, m, CH_2)ppm.

3e: IR(KBr): 2820 (-CH_3), 1670 (C=O), 1585, 1430 (C_6H_6) cm^{-1}; H^1 NMR($CDCl_3$, δ): 7.60(1H, s, ArH), 7.15(1H, d, *J*=7.6 Hz, ArH), 6.95(1H, d, *J*=7.6 Hz, ArH), 2.90(2H, m, CH_2), 3.18(2H, m, CH_2,), 3.80(3H, s, CH_3)ppm.

3f: IR(KBr): 2800 (-CH_3), 1665 (C=O), 1580, 1430 (C_6H_6) cm^{-1}; H^1 NMR($CDCl_3$, δ): 7.68(1H, s, ArH), 7.18(1H, d, *J*=8 Hz, ArH), 7.00(1H, d, *J*=8 Hz, ArH), 2.90(2H, m, CH_2), 3.10(2H, m, CH_2,), 3.68(3H, s, CH_3)ppm.

3g: IR(KBr): 2800 (-CH_3), 1660 (C=O), 1580, 1445 (C_6H_6) cm^{-1}; H^1 NMR($CDCl_3$, δ): 7.56(1H, s, ArH), 7.20(1H, d, *J*=8.8 Hz, ArH), 6.95(1H, d, *J*=8.8 Hz, ArH), 2.87(2H, m, CH_2), 3.02(2H, m, CH_2,), 2.70(3H, s, CH_3)ppm.

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